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10/807,799	03/24/2004	Randall K. Wetzel	CST-214	4415
<div>7590 06/29/2007</div> <div>James Gregory Cullem, Esq. Intellectual Property Counsel CELL SIGNALING TECHNOLOGY, INC. 3 Trask Lane Danvers, MA 01923</div>				
EXAMINER				
DAVIS, MINH TAM B				
ART UNIT		PAPER NUMBER		
1642				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/807,799

Applicant(s)

WETZEL ET AL.

Examiner

MINH-TAM DAVIS

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 April 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) 9-14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8 and 15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 4/16/04; 6/14/05; 1/20/06
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application
- ☐ Other: _____

DETAILED ACTION

Applicant's election without traverse of Group I, claims 1-8, 15 in the reply filed on 04/17/07 is acknowledged.

The restriction requirement of 12/18/06 is still deemed proper and is therefore made FINAL.

Accordingly, group I, claims 1-8, 15 are examined in the instant application.

Specification

The specification is objected to, because the use of the trademarks without being capitalized has been noted in this application, for example, on pages 2-3, 16. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Drawings

If Applicant wants drawings executed in color, Applicant is required to submit a petition, an appropriate fee, and three sets of color drawings or color photographs, as appropriate.

Color photographs and color drawings are not accepted unless a petition filed under 37 CFR 1.84(a)(2) is granted. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and,

unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings and black and white photographs have been satisfied. See 37 CFR 1.84(b)(2).

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claims 1-8 are indefinite for the use of the language "wild type" in claim 1. It is not clear what constitutes wild type, in view of a lack of definition of "wild type" in the specification.
2. Claim 4 is indefinite, for the use of the language "suitable". It is not clear what constitutes suitability of the claimed antibody for detecting the fusion protein.

Claim Rejections - 35 USC § 112, First Paragraph, Deposit Requirement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 8 is rejected under the deposit rule requirement, because one cannot predict the characteristics required by the hybridoma cell line, having Accession No: PTA-5851 without its public availability. A deposit for patent purposes of the hybridoma cell line PTA-5851 is required to enable the invention of claim 8, because it is not clear that the cell lines possessing the identical structure and functional properties of those of the hybridoma cell line PTA-5851 are known and publicly available or can be reproducibly isolated without undue experimentation. Without a publicly available deposit of the hybridoma cell line PTA-5851, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of the hybridoma cell line PTA-5851, which produces chemically and functionally distinct antibodies is an unpredictable event. For example, very different V_H chains (about 50% homologous) can combine with the same V_K chain to produce antibody-binding sites with nearly the same size, shape, antigen specificity, and affinity. A similar phenomenon can also occur when different V_H sequences combine with different V_K sequence to produce antibodies with very similar properties. The results indicate that divergent variable region sequences, both in and out of the complementary determining regions, can be folded to form similar binding contours, which result in similar immunochemical characteristics (William E. Paul, ed., 3rd ed. 1993, Fundamental Immunology, p. 242). The hybridoma cell line PTA-5851 is distinct and having unique properties; and one of ordinary skill in the art would be forced into undue

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experimentation in order to make the claimed hybridoma cell line PTA-5851, in view of the lack of exemplary materials and in view of the unpredictability associated with obtaining the exact species repeatedly. A deposit of the hybridoma cell line PTA-5851 would satisfy the requirements of 35 USC 112 first paragraph in this case. See CFR 1.801-CFR 1.809.

If a deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the desposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required.

In addition, the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803-1.809 for additional explanation of these requirements.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description

Claims 1-8, 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses that the claimed antibody does not recognize the c-ABL, or BCR (p.24, last paragraph). The specification discloses that the BCR-ABL fusion protein presently may be detected using antibody against either the wild type BCR or c-ABL protein (p. 3, lines 24-26).

“Wild type BCR” or **“wild type c-ABL”**, without being accompanied by a sequence identification number encompasses a genus of BCR or ABL sequences with unknown structure and function, in view that it is not clear what wild type BCR or wild type c-ABL means.

The art does not disclose structure of the claimed numerous BCR or ABL sequences.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that “[a] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials.” *Id.* At 1567, 43 USPQ2d at 1405. The court also stated that

a generic statement such as “vertebrate insulin cDNA” or “mammalian insulin cDNA” without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. *Id.* At 1568, 43 USPQ2d at 1406. The court

concluded that “naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.” Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. “A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.” Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that □the written description requirement can be met by “show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristicsi.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.” Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here.

In this case, the specification does not describe wild type BCR or wild type c-ABL in a manner that satisfies either the standards as shown in the example of Lilly or Enzo. The specification does not provide sufficient structure or common structure to support the broad breath of the claimed genus. Nor is there any functional characteristics coupled with a known or

disclosed correlation between structure and function. This does not provide a description of wild type BCR or wild type c-ABL, that would satisfy the standard as shown in the example of Enzo.

The specification also fails to describe wild type BCR or wild type c-ABL, by the standards shown in the example in Lilly. The specification fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

The specification does not provide an adequate written description of wild type BCR or wild type c-ABL, that is required to practice the claimed invention. Thus, the specification does not meet the 112, first paragraph written description requirement, and one of skill in the art would reasonably conclude that Applicant did not have possession of the claimed wild type BCR or wild type c-ABL at the time the invention was made.

Claim Rejections - 35 USC § 112, First Paragraph, Enablement

Claims 1-7, 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

1. It is noted that wild type BCR or wild type c-ABL is an **essential material** for the claimed composition. However, the specification only refers to a published reference when describing wild type BCR or wild type c-ABL (p.3, lines 24-26). MPEP 608.01 teaches that

incorporation of **essential material** in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference (see 37 CFR 1.57). The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. In re Hawkins, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); In re Hawkins, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); In re Hawkins, 486 F.2d 577, 179 USPQ 167 (CCPA 1973) (see MPEP 6.19 and 6.19.01) . In other words, Applicant is required to submit a paper copy and a computer readable form copy of the wild type BCR or wild type c-ABL sequence cited in the published reference as referred to in the specification, and a statement that the content of the paper and computer readable copies are the same, and include no new matter, as required by 37 CFR 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). Applicant is also required to submit an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application.

2. Claims 1-7, 15 are also rejected under 112, first paragraph for lack of enablement for **“wild type BCR” or “wild type c-ABL”**.

The disclosure in the specification has been set forth above.

“Wild type BCR” or “wild type c-ABL”, without being accompanied by a sequence identification number encompasses a genus of BCR or ABL sequences with unknown structure and function, in view that it is not clear what wild type BCR or wild type c-ABL means.

Applicants have not shown how to make the claimed numerous BCR or ABL sequences, in view that protein chemistry is probably one of the most unpredictable areas of biotechnology and that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. For example, Bowie et al (Science, 1990, 257 : 1306-1310) teach that an amino acid sequence encodes a message that determine the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instruction of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex (col.1, p.1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitution can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col.2, p.1306). The 3- dimensional folding of the native molecule however is of significant importance in an antibody response, because epitopes of an antibody could be linear and/or conformational. For example, Roger, I et al, 1988, Bioscience Reports, 8(4): 359-368, teach that several epitopes of p85 glycoprotein are conformational determinants and are destroyed by reduction of said glycoprotein (abstract). The references thus demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the characteristics or three

dimensional structure of a protein, and consequently the binding and characteristics of the antibodies specific for said protein.

MPEP 2164.03 teaches that “the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling.”

Given the above unpredictability, and in view of the complex nature of the invention, a lack of sufficient disclosure in the specification, and little is known in the art concerning the claimed invention, it would have been undue experimentation for one of skill in the art to practice the claimed invention, that is commensurate in scope of the claims.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SHANON FOLEY can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MINH TAM DAVIS
June 18, 2007

/Larry R. Helms/

Supervisory Patent Examiner